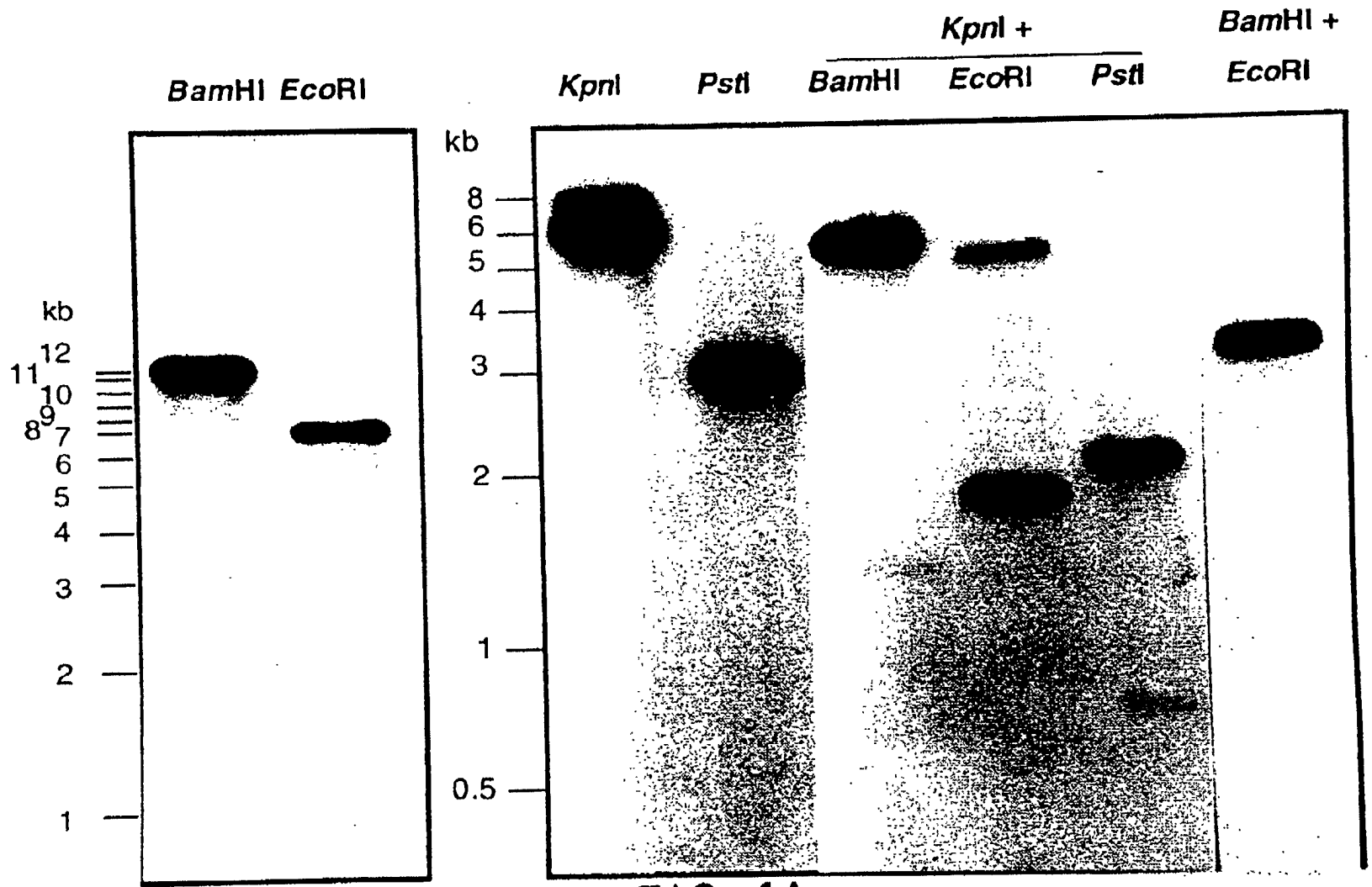
BamHI EcoRI
kb
12
11
10
9
8
7
6
5
4
3
2
1
KpnI
PstI
KpnI +
BamHI
EcoRI
PstI
BamHI +
EcoRI
kb
8
6
5
4
3
2
1
0.5

FIG. 1A

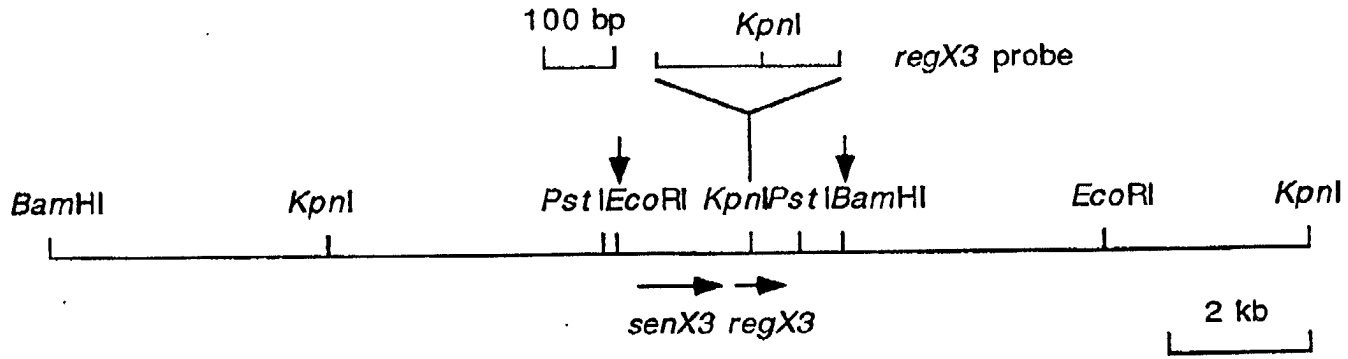
100 bp
KpnI
regX3 probe
BamHI
KpnI
PstI EcoRI KpnI PstI BamHI
EcoRI
KpnI
senX3 regX3
2 kb

FIG. 1B

```
     GAATTCCGCTGCGCTACGACCTGGATTCCGCGATGAGGCCGCTGGTGCGCGGTGG 55
       I  P  L  R  Y  D  L  D  S  A  M  R  P  L  V  R  G  G
     → PgmY

TACGTATCTGGACCCGGAGGCGGCAGCCGCCGGCGCCGCCGCGGTGGCCGGCCAGGGCCG 115
 T  Y  L  D  P  E  A  A  A  A  G  A  A  A  V  A  G  Q  G  R

CGGGTAATTGTTTGAGATCCCACCTGCCGGCGGTTTCGGCGGCTGATGGTGTGCTTTGGT 175
 G
      ──────→  ←──────
GCGCTGTTTGCCAAACAGCATGTGAACGGTAACCGAACAGCTGTGGCGTAGTGTGTGACT 235

TGTCCGATTTTGGCCTTGCCGCGCTAGGGCGACGTTCACCGGATTTGTAGGATTTTCCTT 295
                                              SD
GTGACTGTGTTCTCGGCGCTGTTGCTGGCCGGGGTTTTGTCCGCGCTGGCACTGGCCGTC 355
M  T  V  F  S  A  L  L  L  A  G  V  L  S  A  L  A  L  A  V   20
SenX3 →

GGTGGTGCTGTTGGAATGCGGCTGACGTCGCGGGTCGTCGAACAGCGCCAACGGGTGGCC 415
G  G  A  V  G  M  R  L  T  S  R  V  V  E  Q  R  Q  R  V  A   40

ACGGAGTGGTCGGGAATCACGGTTTCGCAGATGTTGCAATGCATTGTCACGCTGATGCCG 475
T  E  W  S  G  I  T  V  S  Q  M  L  Q  C  I  V  T  L  M  P   60

CTGGGCGCCGCGGTGGTGGACACCCATCGCGACGTTGTCTACCTCAACGAACGGGCCAAA 535
L  G  A  A  V  V  D  T  H  R  D  V  V  Y  L  N  E  R  A  K   80

GAGCTAGGTCTGGTGCGCGACCGCCAGCTCGATGATCAGGCCTGGCGGGCCGCCCGGCAG 595
E  L  G  L  V  R  D  R  Q  L  D  D  Q  A  W  R  A  A  R  Q  100

GCGCTGGGTGGTGAAGACGTCGAGTCCGACCTGTCGCCGCGCAAGCGGTCGGCCACGGGT 655
A  L  G  G  E  D  V  E  S  D  L  S  P  R  K  R  S  A  T  G  120

CGATCCGGGCTATCAGTGCATGGGCATGCCCGGTTGCTGAGCGAGGAAGACCGCCGGTTC 715
R  S  G  L  S  V  H  G  H  A  R  L  L  S  E  E  D  R  R  F  140

GCCGTGGTGTTCGTGCACGACCAGTCGGATTATGCGCGGATGGAGGCGGCTAGGCGTGAC 775
A  V  V  F  V  H  D  Q  S  D  Y  A  R  M  E  A  A  R  R  D  160

TTCGTGGCCAACGTCAGTCACGAGCTCAAGACGCCCGTCGGTGCCATGGCTCTACTCGCC 835
F  V  A  N  V  S  H  E  L  K  T  P  V  G  A  M  A  L  L  A  180
                  ↑ H
```

FIG.2

WO 96/23895 PCT/US96/02202

```
GAGGCGCTGCTGGCGTCGGCCGACGACTCCGAAACCGTTCGGCGGTTCGCCGAGAAGGTG 895
E  A  L  L  A  S  A  D  D  S  E  T  V  R  R  F  A  E  K  V   200

CTCATTGAGGCCAACCGGCTCGGTGACATGGTCGCCGAGTTGATCGAGCTATCCCGGCTA 955
L  I  E  A  N  R  L  G  D  M  V  A  E  L  I  E  L  S  R  L   220

CAGGGCGCCGAGCGGCTACCCAATATGACCGACGTCGACGTCGATACGATTGTGTCGGAA 1015
Q  G  A  E  R  L  P  N  M  T  D  V  D  V  D  T  I  V  S  E   240

GCGATTTCACGCCATAAGGTGGCGGCCGACAACGCCGACATCGAAGTCCGCACCGACGCG 1075
A  I  S  R  H  K  V  A  A  D  N  A  D  I  E  V  R  T  D  A   260

CCCAGCAATCTGCGGGTGCTGGGCGACCAAACTCTGCTGGTTACCGCACTGGCAAACCTG 1135
P  S  N  L  R  V  L  G  D  Q  T  L  L  V  T  A  L  A  N  L   280
                                              N

GTTTCCAATGCGATTGCCTATTCGCCGCGCGGGTCGCTGGTGTCGATCAGCCGTCGCCGT 1195
V  S  N  A  I  A  Y  S  P  R  G  S  L  V  S  I  S  R  R  R   300

CGCGGTGCCAACATCGAGATCGCCGTCACCGACCGGGGCATCGGCATCGCGCCGGAAGAC 1255
R  G  A  N  I  E  I  A  V  T  D  R  G  I  G  I  A  P  E  D   320
                          G1

CAGGAGCGGGTCTTCGAACGGTTCTTCCGGGGGGACAAGGCGCGCTCGCGTGCCACCGGA 1315
Q  E  R  V  F  E  R  F  F  R  G  D  K  A  R  S  R  A  T  G   340
             F

GGCAGCGGACTCGGGTTGGCCATCGTCAAACACGTCGCGGCTAATCACGACGGCACCATC 1375
G  S  G  L  G  L  A  I  V  K  H  V  A  A  N  H  D  G  T  I   360
G2

CGCGTGTGGAGCAAACCGGGAACCGGGTCAACGTTCACCTTGGCTCTTCCGGCGTTGATC 1435
R  V  W  S  K  P  G  T  G  S  T  F  T  L  A  L  P  A  L  I   380

GAGGCCTATCACGACGACGAGCGACCCGAGCAGGCGCGAGAGCCCGAACTGCGGTCAAAC 1495
E  A  Y  H  D  D  E  R  P  E  Q  A  R  E  P  E  L  R  S  N   400

AGGTCACAACGAGAGGAAGAGCTGAGCCGATGACCTGCGCCGACGACGATGCAGAGCGTA 1555
R  S  Q  R  E  E  E  L  S  R  410
```

FIG. 2

(cont.)

WO 96/26206 PCT/US96/02802

```
GCGATGAGGTGGGGGCACCACCCGCTTGCGGGGGAGAGTGGCGCTGATGACCTGCGCCGA 1615

CGACGATGCAGAGCGTAGCGATGAGGTGGGGGCACCACCCGCTTGCGGGGGAGAGTGGCG 1675

CTGATGACCAGTGTGTTGATTGTGGAGGACGAGGAGTCGCTGGCCGATCCGCTGACGTTT 1735
   M  T  S  V  L  I  V  E  D  E  E  S  L  A  D  P  L  T  F    19
   RsgX3 →
CTGCTGCGCAAGGAGGGCTTTGAGGCCACGGTGGTGACCGATGGTCCGGCAGCTCTCGCC 1795
L  L  R  K  E  G  F  E  A  T  V  V  T  D  G  P  A  A  L  A    39

GAGTTCGACCGGGCCGGCGCCGACATCGTCCTGCTCGATCTGATGCTGCCTGGGATGTCG 1855
E  F  D  R  A  G  A  D  I  V  L  L  D  L  M  L  P  G  M  S    59
                                    ↑

GGTACCGATGTATGCAAGCAGTTGCGCGCTCGGTCCAGCGTTCCGGTGATCATGGTGACC 1915
G  T  D  V  C  K  Q  L  R  A  R  S  S  V  P  V  I  M  V  T    79

GCCCGGGATAGCGAGATCGACAAGGTGGTCGGCCTGGAGCTGGGCGCTGACGACTACGTG 1975
A  R  D  S  E  I  D  K  V  V  G  L  E  L  G  A  D  D  Y  V    99

ACCAAGCCCTATTCGGCACGCGAGTTGATCGCACGCATCCGCGCGGTGCTGCGCCGTGGC 2035
T  K  P  Y  S  A  R  E  L  I  A  R  I  R  A  V  L  R  R  G   119

GGCGACGACGACTCGGAGATGAGCGATGGCGTGCTGGAGTCCGGGCCGGTTCGCATGGAT 2095
G  D  D  D  S  E  M  S  D  G  V  L  E  S  G  P  V  R  M  D   139

GTGGAGCGCCATGTCGTCTCGGTGAACGGTGACACCATCACGCTGCCGCTCAAGGAGTTC 2155
V  E  R  H  V  V  S  V  N  G  D  T  I  T  L  P  L  K  E  F   159

GACCTGCTGGAATACCTGATGCGCAACAGCGGGCGGGTGTTGACTCGCGGACAACTGATC 2215
D  L  L  E  Y  L  M  R  N  S  G  R  V  L  T  R  G  Q  L  I   179
```

FIG. 2

(cont.)

```
GACCGGGTCTGGGGTGCGGACTACGTGGGCGACACCAAGACGCTCGACGTCCATGTCAAG 2275
D  R  V  W  G  A  D  Y  V  G  D  T  K  T  L  D  V  H  V  K   199

CGGCTGCGCTCCAAGATCGAAGCCGACCCGGCTAACCCGGTTCACTTGGTGACGGTGCGC 2335
R  L  R  S  K  I  E  A  D  P  A  N  P  V  H  L  V  T  V  R   219

GGGCTGGGCTACAAACTCGAGGGCTAGCGGACGCCGACAACCTTGGCGACTGTCTGGTCG 2395
G  L  G  Y  K  L  E  G  227

GCTACGGCCAGTGCCATCGCCATGATGGACAGCTGCGGGTTCACTTCCGGGCAGCTGGGC 2455

AGGATCGAGGCGTCGGCAACCCACACGCCCTCGACGCCGCGCAGCCGGCCCGTCGCGTCG 2515

ACCGGACAAAGCTGCTCGTCGGCGCCGGCGGCCGCGGTGCCCGTCGGATGGAAGGCGGCC 2575

AGGTGCAGGCTTCTGGGGTTGGCTCGGCGCAGCACATCCTGCAGCTCGGGCAGGGACCGC 2635

ATCGGTGGGGCGCCGGGGATACCGGTCAGCACCTCCACCGCGCCGGCGGCAAAGAACAGC 2695

CGGCCAATGGCCTGCAGCGCGACCCGTAGCTTGGCGATCTCACCTGGAGCTATGTCATAG 2755

CGCACCACCGTCTCGCCGCGCACCGACCGCACCGTGCCGACGCCCCGATCGGCCACCATC 2815

GCCCCGAATGTTGCGATCTGCGGCGCCCGGTCGAGCCAGCGGAGCAGCTCGGCCCCGTAG 2875

CCGGGGAAGACCATCGACCCCATGCCCGGCGGTGTGGAGGTGGCCTCGATCAGCACGCCG 2935

TCGGATTCGTGAAACTCGTGAACCGCCGCGCTCTGCAGCACCCCGCGCCACGCGAAGACG 2995

TCGTCGTCGAAGAGCCCGGCCAGCATAGTTGCCGGGTGCAGCGCAAGGTTGTGGCCCAGT 3055

CGCGGTGCCCACCAAGACCGCTGCGCCGCAACAGCCCTGGCGTCTCCGTCGCACCGGCGG 3115

CGACGACGACCGCGTCGGCCAGCACGTCGAGTGTGGTGCCGTCGGGCCGGCGGGCTCGCA 3175

CGCCATAGGCCCGCCCGGCGCGGTGCAGGATCC 3208
```

FIG.2

(cont.)

EP 0 396 208 B2

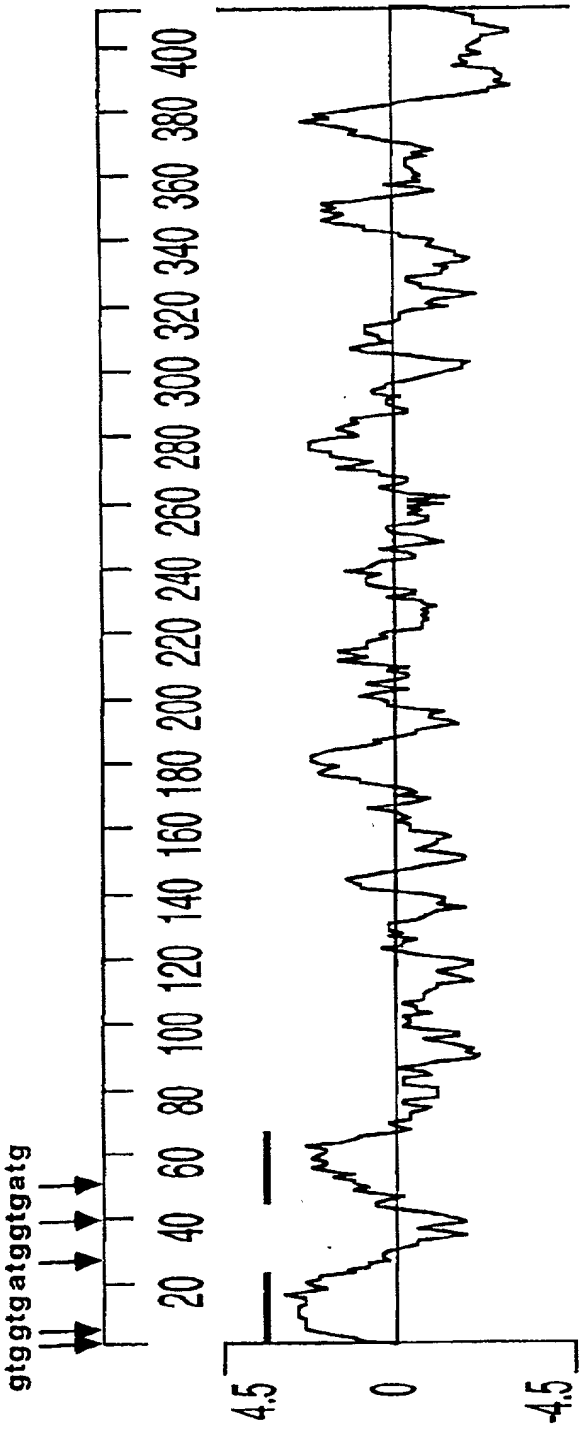
gtggtgatggtgatg
20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400
4.5
0
-4.5

FIG. 3

A. BCG

```
GCT GAG CCG ATG ACC TGC GCC GAC GAC GAT GCA GAG CGT AGC GAT
          M   T   C   A   D   D   D   A   E   R   S   D
senX3 → L   S   R   *
```

```
GAG GTG GGG GCA CCA CCC GCT TGC GGG GGA GAG TGG CGC TGA TGA
E   V   G   A   P   P   A   C   G   G   E   W   R   *   *
                                                    M   T
```

```
CCT GCG CCG ACG ACG ATG CAG AGC GTA GCG ATG AGG TGG GGG CAC

  C   A   D   D   D   A   E   R   S   D   E   V   G   A   P

CAC CCG CTT GCG GGG GAG AGT GGC GCT GAT GAC CAG TGT
                                    M   T   S   V → regX3
  P   A   C   G   G   E   W   R   *   *
```

B. *Mycobacterium tuberculosis*

```
GCT GAG CCG ATG ACC TGC GCC GAC GAC GAT GCA GAG CGT AGC GAT
          M   T   C   A   D   D   D   A   E   R   S   D
senX3 → L   S   R   *
```

```
GAG GTG GGG GCA CCA CCC GCT TGC GGG GGA GAG TGG CGC TGA TGA
E   V   G   A   P   P   A   C   G   G   E   W   R   *   *
                                                    M   T
```

```
CCT GCG CCG ACG ACG ATG CAG AGC GTA GCG ATG AGG TGG GGG CAC

  C   A   D   D   D   A   E   R   S   D   E   V   G   A   P

CAC CCG CTT GCG GGG GAG AGT GGC GCT GAT GAC CTG CGC CGA CGA
                                    M   T   C   A   D   D
  P   A   C   G   G   E   W   R   *   *
```

```
CGA TGC AGA GCG TAG CGA TGA GGA GGA GTG GCG CTG ATG ACC AGT
                                            M   T   S → regX3
  D   A   E   R   S   D   E   E   E   W   R   *   *
```

FIG. 4

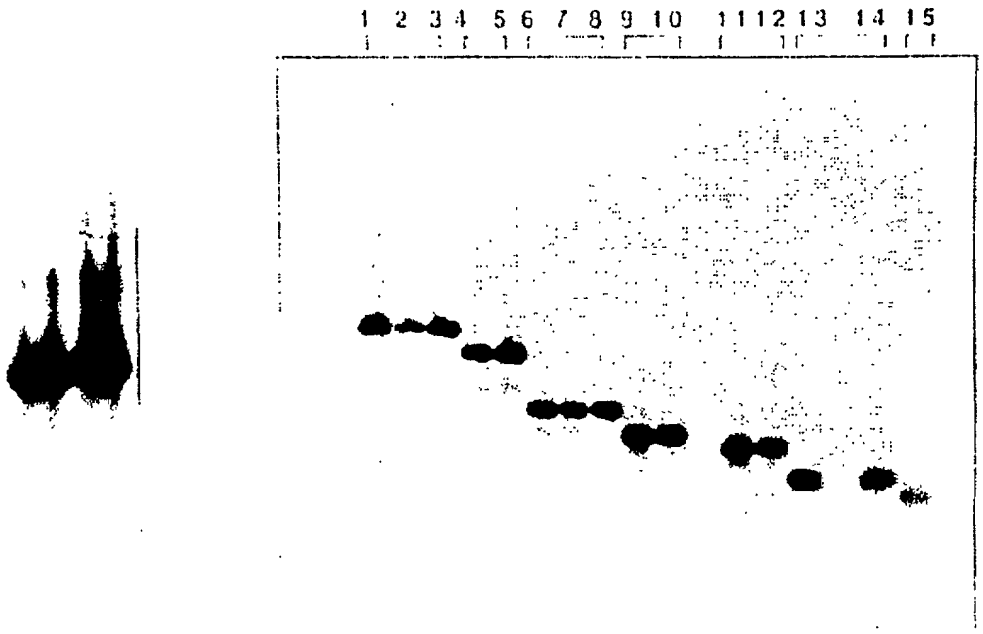

FIG.5

FIG.7

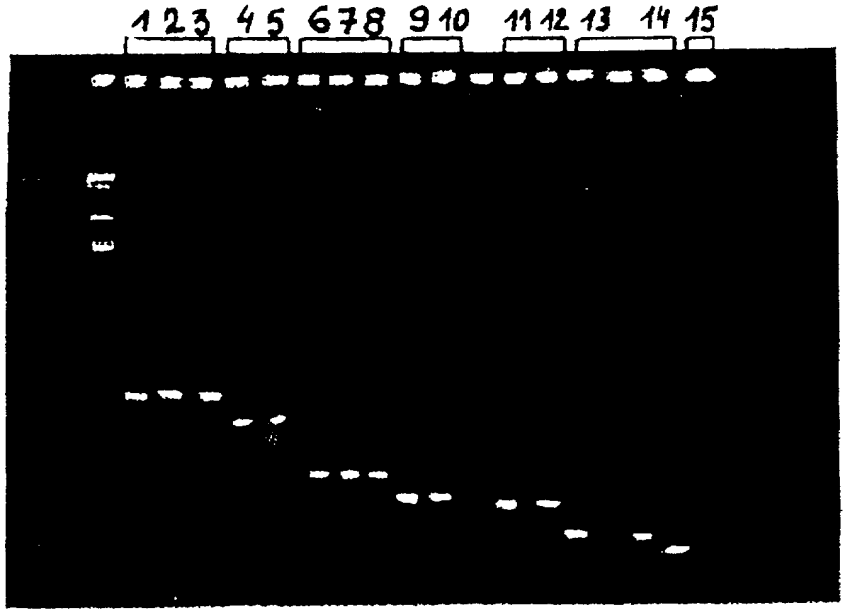

FIG.6

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